(FILE 'HOME' ENTERED AT 12:46:00 ON 10 DEC 2002)

FILE 'MEDLINE, CANCERLIT, BIOTECHDS, EMBASE, BIOSIS' ENTERED AT 12:46:37
ON 10 DEC 2002
L1 12495 S CAMPTOTHECIN
L2 84163 S ADENOVIR?
L3 85 S L2 AND L1
L4 39 DUP REM L3 (46 DUPLICATES REMOVED)
L5 2608 S OLIGO? AND L2
L6 275 S L5 AND DELIVE?
L7 161 DUP REM L6 (114 DUPLICATES REMOVED)
L8 69 S L7 AND ANTISENSE
L9 2265862 S GENE OR TRANSGENE
L10 10 S L6 NOT L9

L4 ANSWER 37 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 74168712 EMBASE
DN 1974168712
TI Inhibition of herpes simplex virus replication by camptothecin.
AU Becker Y.; Olshevsky U.
CS Lab. Molec. Virol., Hebrew Univ. Hadassah Med. Sch., Jerusalem, Israel
SO Israel Journal of Medical Sciences, (1973) 9/11-12 (1578-1581).
CODEN: IJMDAI
DT Journal
FS 037 Drug Literature Index
013 Dermatology and Venereology
047 Virology
030 Pharmacology
LA English
AB The alkaloid camptothecin is a potent inhibitor of tumor cells due to its ability to inhibit DNA and RNA biosynthesis. Camptothecin inhibits the replication of adenovirus DNA in infected cells and causes breaks in preformed viral DNA. Because of these properties, the effect of camptothecin on the replication of herpes simplex virus was investigated. It was found that DNA synthesis in infected cells was inhibited by the alkaloid and morphogenesis of the virus was prevented, although viral structural peptides were synthesized in the infected treated cells. At a concentration which prevented viral DNA synthesis, the major viral structural peptides, II, III, aIV, IV, V, VI and VII, were detected in the camptothecin treated infected cells. This result was assumed to indicate that the transcription of viral mRNA from the parental viral DNA molecules and the translation of the viral mRNA took place in the infected cells in the presence of camptothecin. This finding also indicated that structural viral

L4 ANSWER 19 OF 39 MEDLINE DUPLICATE 13
AN 1999134506 MEDLINE
DN 99134506 PubMed ID: 9933736
TI Water-insoluble **camptothecin** analogues as potential antiviral drugs.
AU Pantazis P; Han Z; Chatterjee D; Wyche J
CS Department of Molecular Biology, Cell Biology and Biochemistry, Brown University, Providence, R.I., USA.. pantazis@brown.edu
SO JOURNAL OF BIOMEDICAL SCIENCE, (1999 Jan) 6 (1) 1-7. Ref: 66
Journal code: 9421567. ISSN: 1021-7770.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199903
ED Entered STN: 19990326
Last Updated on STN: 19990326
Entered Medline: 19990316
AB In addition to being causative agents of infectious diseases in animals and humans, DNA viruses have served as models for the study of eukaryotic molecular mechanisms including replication and transcription. Studies of DNA virus functions utilizing cell-free systems and virus-infected cells in culture, in the presence of the anticancer drug **camptothecin** (CPT), have demonstrated that CPT is a potent inhibitor of replication, transcription and packaging of double-stranded DNA-containing **adenoviruses**, papovaviruses and herpesviruses, and the single-stranded DNA-containing autonomous parvoviruses. CPT inhibits viral functions by inhibiting topoisomer- ase I, a host cell enzyme required for initiation and completion of the viral functions. These findings indicate that CPT analogues could be developed for use as potent drugs against DNA viruses.

peptides are coded by parental viral DNA genomes, in agreement with previous findings. It is of interest that similar results were obtained in HSV infected BSC1 cells treated with cytosine arabinoside (50 .mu.g/ml). Viral DNA replication, as determined by CsCl density gradient centrifugation of the 3H DNA extracted from cytosine arabinoside treated infected cells was completely prevented. The ability of camptothecin to inhibit the synthesis of HSV DNA and to prevent virus morphogenesis resembled its inhibitory effect on adenovirus replication. Under these conditions, the synthesis of viral structural peptides occurred. This indicates that the viral peptides are synthesized according to mRNA species transcribed from the parental DNA genomes. A similar phenomenon was found in HSV infected cells treated with 2 inhibitors of DNA replication: hydroxyurea and cytosine arabinoside.

L4 ANSWER 35 OF 39 CANCERLIT
AN 75805667 CANCERLIT
DN 75805667
TI CAMPTOTHECIN.
AU Horwitz S B
CS No affiliation given.
SO Handb Exp Pharmakol, (1974) 38 (2) 649-656.
DT Book; (MONOGRAPH)
LA English
FS Hierarchical Classification of Proteins
EM 197610
ED Entered STN: 19941107
Last Updated on STN: 19941107
AB Investigations of the cytotoxic plant alkaloid camptothecin are described. Camptothecin has potent antitumor properties in experimental animals. In an early clinical trial, camptothecin was effective in melanoma and advanced gastrointestinal carcinoma; subsequent studies, however, showed intolerable drug toxicity with only two objective responses in 61 pts with gastrointestinal carcinoma and none among 15 pts with disseminated melanoma. The compound reversibly inhibits DNA and ribosomal RNA synthesis in HeLa cells while permitting continued synthesis of transfer RNA and short nucleoplasmic RNA. Human lymphocytes treated during S-phase failed to divide even after removal of the drug, and the DNA isolated from treated HeLa cells had a lower sedimentation constant in alkaline sucrose gradients than DNA from untreated cells. Camptothecin also inhibits replication of adenovirus and vaccinia virus and appears to be a useful new tool for the study of macromolecular synthesis in animal cells and their DNA viruses. (43 refs)

L4 ANSWER 32 OF 39 MEDLINE DUPLICATE 21

AN 90080164 MEDLINE
DN 90080164 PubMed ID: 2152835
TI Topoisomerase I and II cleavage of adenovirus DNA in vivo: both topoisomerase activities appear to be required for adenovirus DNA replication.
AU Schaack J; Schedl P; Shenk T
CS Department of Biology, Howard Hughes Medical Institute, Princeton, New Jersey.
NC CA 41086 (NCI)
SO JOURNAL OF VIROLOGY, (1990 Jan) 64 (1) 78-85.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199001
ED Entered STN: 19900328
Last Updated on STN: 19970203
Entered Medline: 19900122
AB Sites of topoisomerase I and II cleavage across large portions of the adenovirus type 5 genome were mapped by using the drugs camptothecin and VM26, respectively. These drugs prolong the half-lives of the covalent DNA-protein intermediates in which the DNA is transiently cleaved, and so treatment with protein denaturants after exposure to the drugs leads to DNA strand scission at the site of topoisomerase cleavage. Strong topoisomerase II cleavage sites occurred in clusters throughout the regions examined, including both transcribed regions and transcriptional control regions. The efficiency of topoisomerase II cleavage increased as the rate of adenovirus DNA replication increased and then decreased with the decreasing rate of replication late in the infection cycle. The increase was not dependent on expression of the E1A gene, whose products activate transcription of the early viral genes. Positions of topoisomerase II cleavage sites did not vary during the infection. Topoisomerase I cleavage sites were also found throughout the examined regions, with the strongest sites occurring near the ends of the transcription units. Topoisomerase I cleavage in the E1 region occurred much more frequently than topoisomerase II cleavage, was not dependent on E1A gene expression, and remained at a similar level from the early viral phase into the late viral phase. Treatment of infected cells with either drug prevented efficient replication of adenovirus DNA. Inhibition of topoisomerase I activity led to an immediate cessation of adenovirus DNA replication, while inhibition of topoisomerase II blocked replication only after completion of approximately one additional round.

L4 ANSWER 31 OF 39 MEDLINE DUPLICATE 20
AN 90112638 MEDLINE
DN 90112638 PubMed ID: 2153235
TI Involvement of topoisomerases in replication, transcription, and packaging of the linear adenovirus genome.
AU Wong M L; Hsu M T
CS Department of Microbiology, Mount Sinai School of Medicine of City University of New York, New York 10029-6574.
SO JOURNAL OF VIROLOGY, (1990 Feb) 64 (2) 691-9.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199002
ED Entered STN: 19900328
Last Updated on STN: 19970203
Entered Medline: 19900214
AB The role of topoisomerases in the replication of human adenovirus type 5 was investigated with topoisomerase inhibitors. Both topoisomerase I and topoisomerase II inhibitors blocked adenovirus replication when added at the time of infection. Both types of inhibitors induced strand cleavages at specific sites in the adenovirus early templates. The cleavage sites were mapped near the 5' and 3' ends of the genes transcribed early during infection. At late times after infection, camptothecin, a topoisomerase I inhibitor, inhibited adenovirus DNA replication and induced the formation of single- and double-stranded fragments with breakpoints located at defined regions of the viral genome. The topoisomerase II inhibitors, VP-16 (etoposide) and ellipticine, did not block adenovirus DNA replication and did not induce an appreciable amount of double-strand cleavages in the newly synthesized DNA. On the other hand, VP-16 promoted double-strand cleavages at specific sites of nonreplicating adenovirus DNA. The packaging of adenovirus DNA into virus particles, which contain supercoiled adenovirus DNA (M.-L. Wong and M.-T. Hsu, Nucleic Acids Res. 17:3535-3550, 1989), was inhibited by the topoisomerase II inhibitors. Transcription of adenovirus major late genes was inhibited by both topoisomerase I and topoisomerase II inhibitors. In addition, camptothecin caused a premature termination of major late transcription. Electron microscopic analysis showed that adenovirus templates late after infection were arranged in topologically constrained loop domains. Together, these data provide evidence for the requirement of topoisomerase activities in the replication, transcription, and packaging of the linear adenovirus genome.